REMARKS / ARGUMENTS

Claims 1-12, 14 and 16-33 are currently pending. Claim 1 has been amended to place the subject matter in condition for allowance. Claim 12 has also been amended to delete the term "prophylaxis" for the purposes of expediting prosecution. In view of the foregoing amendments and remarks, reconsideration, a withdrawal of all rejections and a Notice of Allowability are respectfully solicited.

Claims 1-12, 14 and 16-33 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement. The Action indicates that solvates as recited by these claims is not enabled. Among various points, the Action states that the specification does not provide any teaching or guidance with respect to solvate preparation, and also does not give any examples of preparing solvates. Applicant respectfully traverses each and every aspect of this rejection.

It is respectfully submitted one of ordinary skill in the art is able prepare solvates of the claimed compounds without any undue experimentation and thus such solvates are fully enabled. The claims of the invention are primarily directed to novel phenethanolamine derivatives, methods of using the same and processes of preparing the same. The Office has not raised an enablement issue with respect to making and using such compounds. As long recognized in the art, solvates are well-known derivatives of such compounds. Given that Applicants have enabled one of ordinary skill in the art to prepare the claimed compounds, one of ordinary skill in the art can readily extrapolate such teachings to form solvates from such compounds. Clearly preparation of such solvates does not constitute undue experimentation.

The law is clear on this issue. "[A] specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing the subject matter sought to be patented ***must*** be taken as in compliance with the enabling requirement of the first paragraph of § 112 *unless* there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support."

In re Marzocchi, 439 F.2d 220, 223 (1971) (emphasis added). In the case at hand, the Office has offered nothing, save subjective opinion, that would cast doubt as to the enablement of making solvates of the claimed compounds. Accordingly, the Office must accept Applicants' specification as being enabling for making solvates of the claimed compounds. A withdrawal of this rejection is therefore respectfully solicited.

The Action also states that Claims 12, 14 and 20-22 directed to methods of treatment are not enabled. The Action alleges that IC50 data under 1 μM using *in vitro* assay needs to be presented in affidavit form. The Action then proceeds to state:

> "Secondly, it is well known in the art that *in vitro* activity does not necessarily always correlate with *in vivo* activity of a compound since unlike *in vitro*, *in vivo* activity is influenced by numerous factors such as absorption, metabolism, presence of enzymes, hormones, etc. There is no teaching in the prior art that structurally closely related compounds having agonist activity at beta 2 adrenoreceptors *in vitro* are well known to have therapeutic utility in treating any disorder following their *in vivo* administration. There are no working examples present showing efficacy of instant compounds in known animal models of any disorder where hypoactivity of beta 2 adrenoreceptors is implicated. The instant compounds of formula (I) encompasses hundreds of thousands of compounds based on the values of R1-R5, m, n and Ar and therefore, in absence of such teachings, guidance, presence of working examples and prior art, it would require undue experimentation to demonstrate efficacy of instant compounds in known animal models of every known disorder where hypoactivity of beta 2 adrenoreceptors is implicated and hence their utility for treating but not prophylaxis of these disorders."
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> (page 4 of the Action)

Applicants respectfully traverse each and every aspect of this rejection.

First, the Office states that the IC50 data under 1 μM using *in vitro* assay needs to be in affidavit form. Applicants respectfully disagree, and submit that there is nothing requiring such. Data may be presented in the patent specification in accordance with long-standing patent drafting procedure. See e.g., MPEP 608.01(p).

Second, the Office alleges, in support of lack of enablement of the method of treatment claims, that *in vitro* activity "does not necessarily always correlate" with *in vivo* activity of a compound, and that compounds having activity at beta 2 adrenoreceptors *in vitro* are well known to have therapeutic utility in treating any disorder following their *in vivo* administration. Applicants disagree with the analysis of the Office. In particular, the Office's analysis does not properly follow precedent pertaining to the presumption of enablement and the burden of the Office to correctly question such. Again, Applicants draw the Office's attention to precedent articulated by *In re Marzocchi* which requires the Office to accept Applicants' disclosure as being enabling. Moreover, asserting, as the Office has here, that *in vitro* activity "does not necessarily always correlate" with *in vivo* activity, does not discharge the burden of the PTO. On this point, the Office is seemingly requesting that a precise correlation be established between the activity of *in vitro* and *in vivo* data. As set forth in MPEP 2164.02, and in clear and direct contrast to the position of the Office, a "rigorous or an invariable exact correlation" between *in vitro and in vivo* data "is not required' to establish enablement with respect to claims relating to method of use. A reasonable correlation is all that is necessary. It is submitted that one of ordinary skill in the art would still reasonably believe that the IC50 data would enable one of ordinary skill in the art to conclude that the claims in question are enabled for the treatment of a clinical condition in a mammal for which a selective β_2-adrenoreceptor agonist is indicated. Thus, such data unquestionably fulfills the enablement requirement.

With respect to the enablement issue regarding a method for the prophylaxis of a clinical condition, Applicants believe that such an element is enabled. Nonetheless, for the purposes of expediting prosecution, this subject matter has been deleted. It is noted that the term "treatment" may be considered to encompass maintenance treatment, eg. ADVAIR DISKUS® is indicated for the maintenance treatment of asthma in patients 4 years of age and older as well as the maintenance treatment of airflow obstruction and for the

treatment of COPD associated with chronic bronchitis[1]. Moreover, in conjunction with the treatment of asthma, the National Institute of Health indicates that long-term control medicines may be taken every day, usually over long periods of time, to prevent symptoms and asthma episodes or attacks. See eg.,
http://www.nhlbi.nih.gov/health/dci/Diseases/Asthma/Asthma_Treatments.html

In view of the above, a withdrawal of all rejections under 35 U.S.C. § 112, first paragraph, is respectfully solicited.

The Office makes a number of rejections under 35 U.S.C. § 102(b). Claims 1, 3, 5-7, 12, 14 and 17-27 are rejected as being anticipated by Bron, WO 95/19336, Claims 1-3, 5-9, 12, 14 and 16-33 are rejected as being anticipated by Skidmore, GB 2140800, and Claims 1, 3, 5, 7, 12, 14 and 17-22 are rejected as being anticipated by Bradshaw, GB 2230523. Applicants respectfully traverse each and every aspect of this rejection. It is submitted that the claims as now amended are not anticipated by any of these cited references. The compounds of the present invention solely encompass benzenesulfonamides in the manner recited by the claims. A withdrawal of these rejections is therefore respectfully solicited.

The points of the Action being addressed in full, a Notice of Allowability is respectfully solicited.

Respectfully submitted,

Dated: June 13, 2007

/Robert J. Smith/
Robert J. Smith
Attorney for Applicant
Reg. No. 40,820
Tel. (919) 483-9616
Fax. (919) 483-7988

[1] ADVAIR DISKUS® 250/50 is the only strength approved for treating COPD associated with chronic bronchitis